

APPENDIX 1. GLOSSARY OF TERMS AND ACRONYMS

Term/acronym	Definition
Actimetry	The measurement of accelerations associated with the movement of an actimeter
ADHD	Attention-deficit hyperactivity disorder
Behavioural awakening	Awakening that is registered by the subject by means of a conscious action
BP	Blood pressure
CAP	Cyclic alternating patterns
EBD	Environmental burden of disease
END	Environmental Noise Directive (2002/49/EC)
EEG	Electroencephalogram, recording of electric activity in the brain
ECG	Electrocardiogram, recording of electric activity of the heart
EEG awakening	Transition from a state of sleep to a state of consciousness, as determined by a sleep EEG
Heart rate acceleration	A temporary rise in heart rate relative to the average heart rate assessed shortly before a noise event
HPA axis	Hypothalamus-pituitary-adrenal axis
ICSD	International Classification of Sleep Disorders
IHD	Ischaemic heart disease
Insomnia	Sleeping disorder consistent with an internationally accepted definition (see ICSD), which takes account of difficulty falling or staying asleep, the daytime implications and the duration of the problems
$L_{Aeq,T}$	Exposure to noise for the duration of a given time interval T (a 24-hour period, a night, a day, an evening) is expressed as an equivalent sound pressure level (measured in dB(A)) over the interval in question
L_{Amax}	Maximum outdoor sound pressure level associated with an individual noise event
L_{night}	Refers to the EU definition in Directive 2002/49/EC: equivalent outdoor sound pressure level associated with a particular type of noise source during night-time (at least 8 hours), calculated over a period of a year
Motility onset	The presence of movement in a short time interval, following an interval without movement
Mg	Magnesium
Motility	The presence of movement in a short time interval, as recorded on an actigram
OR	Odds ratio: the ratio of the odds of an event occurring in another group, or to a sample-based estimate of that ratio

Term/acronym	Definition
OSAS	Obstructive sleep apnoea syndrome
OTC	Over-the-counter (medicines sold without prescription)
Polysomnography	The measurement during a subject's time in bed of his or her brain activity by means of EEG, EOG and EMG. The technique involves the use of electrodes to record electrical potentials in the brain
REM	Rapid eye movement (sleep phase)
RR	Relative risk: a ratio of the probability of the event occurring in the exposed group vs. the control (non-exposed) group
SEL	Sound exposure level: equivalent outdoor sound pressure level associated with an individual noise event, with the equivalent level standardized at one second
Sleep disturbance	Disturbance of sleep by night-time noise, as perceived by a subject and described in a questionnaire response or journal entry
Sleep EEG	Graph created using data from EEG scanning during a subject's time in bed, showing the various stages of sleep as a function of time
Sleep fragmentation	Within a sleep period, the frequency and duration of intervals of wakefulness recorded on a sleep EEG or intervals of motility recorded on an actigram
Sleep latency	The length of time taken to fall asleep, i.e. the interval between the point at which a person begins trying to go to sleep or allowing him/herself to go to sleep and sleep inception time
Sleep stage change	Change from a deeper stage of sleep to a less deep stage, as determined by a sleep EEG
SMR	Standardized mortality ratios
SROBD	Sleep related obstructive breathing disorders
SWS	Slow-wave sleep (sleep phase)
UARS	Upper airway resistance syndrome

APPENDIX 2. RELATIONS BETWEEN L_{NIGHT} AND INSTANTANEOUS EFFECTS

STATEMENT 1

Let f be a function of SEL that gives the expected number of instantaneous effects caused by a single event. With a given L_{night} and a given number of events N , the expected number of times that an effect occurs in the night, n , is maximal if all events have equal SEL, provided that $f \circ 10\lg$ is increasing but negatively accelerated.

STATEMENT 2

If

$$n_{\max} = 10^{(L_{\text{night}} - \text{SEL} + 70.2)/10} \cdot f(\text{SEL}),$$

has a maximum over SEL and f is the quadratic function $f(\text{SEL}) = a \text{ SEL}^2 + b \text{ SEL} + c$, then the maximum occurs irrespective of L_{night} at

$$\text{SEL}_0 = 4.34 - A \pm ((A - 4.34)^2 - (c/a) + 8.68A)^{1/2},$$

where $A = b/(2a)$. (Only with + at the place of \pm the value will come in the realistic range of SEL)

STATEMENT 3A

If the shape of the time pattern of the sound level has a block form, then $\text{SEL} = L_{\text{Amax}} + 10\lg(T)$, where L_{Amax} is the maximum sound level (integrated over 1-s) and T is the duration of the noise event in seconds.

STATEMENT 3B

If the sound level increases with rate a (in dB(A)/s) and after time point $t = 0$ decreases with rate $-a$, then $\text{SEL} \approx L_{\text{Amax}} - 10\lg(a) + 9.4$.

APPENDIX 3. ANIMAL STUDIES ON STRESS AND MORTALITY

INTRODUCTION

Is noise a health risk or does it just annoy? This basic question needs to be carefully answered when establishing night noise guidelines. No one will deny that in the case of high noise levels there is a risk of inner ear damage, but what about the moderate levels of environmental noise? To approach this rather difficult question, all available methods must be combined.

1. In animal experiments it is possible to assess the complete causal chain from noise exposure via physiological reactions and biological risk factors to morbidity or even mortality. However, a quantitative application of the results to humans is not possible. Instead, the method is useful in studying the pathomechanisms qualitatively.
2. Experiments on humans are, for ethical reasons, restricted to the study of reversible physiological reactions. But as long as there is no proof that reactions to chronically repeated noise exposures are increasing the risk of specific diseases, the results of such physiological studies are not considered conclusive.
3. Epidemiological studies have the advantage of investigating health effects which are particularly caused by chronic noise exposure although there is no possibility to control all influencing factors. Additionally, epidemiological studies have to be based upon biologically evident hypotheses.

A hypothetical model of noise-induced health effects is shown in Fig. 4.3 in Chapter 4, section 4.5.2 of this report. This model is based on the results of noise experiments with animals and humans. With animal experiments, the whole causal chain from noise exposure to health outcome can be traced as a direct pathway starting with a chronic high level noise exposure which, via endocrine stress reactions, leads, for example, to microcirculatory defects and to manifest hypertension.

Physiological experiments on humans have shown that noise of a moderate level acts via an indirect pathway and has health outcomes similar to those caused by high noise exposures on the direct pathway. The indirect pathway starts with noise-induced disturbances of activities such as communication or sleep. Since we are dealing with night noise guidelines, noise-induced sleep disturbances and any resulting persistent health effects are of primary interest here.

In physiological studies with experimentally changed noise exposure, the increase of arousals and of hormone excretion was studied in sleeping people. If this model is correct then in the cause-effect chain the arousal ought to precede the endocrine reactions. This order was derived from the different reaction times of the effects. While arousals appear within 1 second after a noise stimulus, hormones like catecholamines take several minutes, and cortisol about 10 minutes to be increased. This observation, together with the fact that arousals are evoked by equal or lower noise levels than the corresponding endocrine reactions, confirms the correctness of the model and leads to an important conclusion: noise exposure which does not evoke arousals in sleeping people will not induce adverse health effects.

This conclusion is essential with regard to night noise guidelines. However, the answers to the basic question as to whether certain health risks are connected with

environmental noise must be clarified by epidemiological studies based on noise experiments on both humans and animals.

TYPES OF ANIMAL STUDIES

Noise has often been used as a stressor in animal studies. Even Selye (1953), who introduced the psychophysiological stress concept, used noise stimuli in his animal studies. Most of the modern animal studies testing the pharmacological effects of drugs are carried out with and without various stressors. The typical noise exposure is to short and very intensive sounds. One such example is the study of Diao et al. (2003) who exposed guinea pigs to 4 kHz octave band noise at 115 dB for 5 hours. But these experiments are of little value regarding the noise exposure types in question.

The same is true for another type of animal study concerned with the prevention of noise-induced health effects in wild and domestic animals (for review of the former kind see Fletcher, 1983). One example for the latter kind is the study of Geverink et al. (1998) on stress responses of pigs to transport and lairage sounds.

Since the subject of the present paper is noise-induced health effects in humans, the review addresses only those studies in which animals are used as a model for humans.

The animal model for aural effects in humans has been established in great detail, so that even quantitative transference of results from animals to humans is possible. However, inner ear damage generally occurs at much higher noise levels than the environmental levels under discussion in this paper. Therefore interest focuses on animal models with respect to extra-aural noise effects.

LIMITING ASPECTS OF ANIMAL MODELS

Other than in studies on aural effects, the animal model does not allow quantitative comparisons in studies of extra-aural noise effects. It may, however, be used for the qualitative investigation of pathophysiological mechanisms following exposure to acute and very short sounds. But an animal model for long-term noise effects as caused by chronically repeated noise exposures needs careful planning. First it has to be ensured that stress reactions in both humans and animals when activated by noise exposure are qualitatively comparable. Secondly, the stress effects of chronic noise exposure have to be assessed in humans, and the animal models should be designed correspondingly. However, in the animal model, influences from cortical interconnections have to be excluded as a factor in these noise experiments. Naturally, one cannot expect to establish an animal model for indirect environmental noise effects which in humans may, for example, disturb activities such as verbal communication, which in turn may induce stress hormone increases.

STRESS HORMONES IN NOISE-EXPOSED ANIMALS

HABITUATION

In short-term experiments any kind of exposure to loud noise will cause acute increases of stress hormones. Long-term repeated noise exposure, however, will

cause a certain habituation in the animal. Periodic repetitions of identical noise bursts lead to almost complete habituation. This was probably the main reason why Borg (1981) found no adverse health effects in rats exposed for their whole lives to periodic noise pulses. Therefore, random series of noise pulses are now applied in most long-term studies.

Selye (1974) had already stated that not all stages of a stress response are noxious, especially in the case of mild or brief exposures. Since environmental noise is a mild stressor, adverse health effects are only to be expected under the condition that repeated noise exposures induce long-term stress hormone changes. According to the Allostatic Load Model (McEwen, 1998), the normal response to an environmental stressor such as noise is the physiological activation of the endocrine system enabling the body to cope with the stressor and, after the stress situation is terminated, to shut off the allostatic response.

J.D. HENRY'S MODEL OF BEHAVIOURAL STRESS EFFECTS

On the basis of the available literature on stress effects in animals and humans, Henry (1992) developed a model with regard to different biological effects and health risks associated with different coping styles. He explains that the neuroendocrine response to various challenges and threats varies according to the type and degree of control a mammal can exert over it. This in turn is strongly determined by the animal's previous experience. In general, the sympathetic adrenomedullary system is preferentially activated when the animal displays an active response to escape from or deal with an environmental challenge. This is the fight/flight mode of stress response. The adrenocortical axis is preferentially activated as the subjects become immobile/passive when no control or threat of its loss is experienced. This is the conservation/withdrawal mode of response.

THE NOISE STRESS MODEL

On the basis of noise effect studies in animals and humans (for review see Ising and Braun, 2000), a noise stress model was developed. It describes a differentiation of prevailing "stress hormones" under noise exposure. Predominantly adrenaline – and to a lesser degree noradrenaline – are released from the adrenal medulla as the normal response to novel noise stimuli of moderate intensity. Following long-term noise exposures of moderate intensity habituation will alter the response mode and predominantly noradrenaline is released. As a response to extremely intensive noise, near the inner ear pain threshold, predominantly cortisol is released from the adrenal cortex induced by increased releases of adrenocorticotrophic hormone (ACTH), especially in the case of unexpected noise.

The described differentiation will only be observed under special conditions. Unexpected exposure for three minutes to white noise at 75 dB leads, in dogs that are awake, to increased adrenal secretion of adrenaline and noradrenaline and – following a delayed increase in plasma ACTH – an increase in cortisol secretion (Engeland, Miller and Gann, 1990).

The cortisol response as described is valid for animals and humans in their active phases. During sleep, however, several studies in humans showed cortisol increases under exposure to traffic noise of moderate levels (Maschke, Arndt and Ising, 1995;

Evans et al. 2001; Ising and Ising, 2002; Ising et al., 2004). It was hypothesized that noise stimuli signalling a danger, for example the noise of an approaching lorry, will, during sleep, normally generate a defeat reaction, which includes the release of cortisol from the adrenal cortex. Appropriate studies with sleeping animals after conditioning them – for example with a specific noise stimulus followed by pain – should be carried out to test this hypothesis.

Rats were exposed for a period of 12 hours to low-altitude flight noise – reproduced electro-acoustically once per hour on average at stochastically fluctuating intervals (L_{Amax} 125 dB, 10 dB downtime: 1 s, L_{eq} : 89 dB) (Ising et al., 1991; Ising, 1993). Adrenaline and noradrenaline excretions tended to decrease, whereas plasma cortisol increased significantly. Although in rats corticosterone is secreted rather than cortisol, we will simplify this paper by using cortisol for rats all the same. In this experiment, as well as in all others of our group, normally four rats were kept in one stainless steel cage, which was set on a funnel to collect their urine.

These results show that exposure to noise levels approaching or exceeding the pain threshold of the inner ear leads to endocrine reactions qualitatively different from those induced by less intensive noise.

The different endocrine reactions to acute and chronic noise exposure were studied in rats by Gesi et al. (2002b). They were exposed either to a single (6-hour) session of loud (100 dB(A)) noise, or to the same noise stimulus repeatedly every day for 21 consecutive days. Exposure to noise for 6 hours on one day induced parallel increases in dopamine, noradrenaline and adrenaline concentrations in tissue samples of the adrenal medulla. After 21 days of noise exposure, noradrenaline concentration was significantly higher than in controls, and that of adrenaline decreased significantly. Cortisol was not assessed in this study.

In another subchronic noise experiment, rats were exposed to irregular white noise at 90 dB for 3 and 9 hours per day during 18 and 8 days respectively (van Raaij et al., 1997). In rats with 3 hours of exposure per day the blood concentrations of adrenaline, noradrenaline and cortisol did not differ from controls. Exposure for 9 hours per day, however, resulted in significantly increased concentrations of noradrenaline and cortisol. At the end of the experiment all animals were subjected to restraint stress and their endocrine reactions were assessed. The authors sum up their findings as follows: these results indicate that chronic noise exposure at mild intensities induces subtle but significant changes in hormonal regulation.

The results of another experiment with different levels of random white noise pulses during 45 minutes per hour, 12 hours per day for 8 days demonstrate that cortisol responses to subchronic mild noise exposure do not monotonously increase with the noise levels (Bijlsma et al., 2001). While in rats exposed to 95 dB pulses plasma cortisol concentrations were raised twofold against controls, the exposure to 105 dB pulses did not increase cortisol significantly.

The time dependency of cortisol increase in the blood of rats under exposure to white noise (100 dB, 6 hours per day for 21 days) was examined by Gesi et al. (2001). The authors found a progressive increase in cortisol which reached a plateau 9 days from the beginning of exposure.

In summing up the results of these studies we can reach the following conclusions.

- Acute exposure to unexpected and novel noise of moderate intensities leads to activation of both the sympathetic adrenal-medullary system with increased secretion of adrenaline and noradrenaline, and the HPA axis with increased secretion of ACTH and of cortisol from the adrenal cortex.
- Under chronic exposure to unpredictable noise, adrenaline secretion is reduced to normal or subnormal values while noradrenaline and ACTH/cortisol concentrations remain increased.
- Extremely intensive unpredictable noise near the inner ear pain threshold triggers, in mammals that are awake, a defeat reaction with increases of ACTH/cortisol while the catecholamines adrenaline and noradrenaline remain normal or are slightly decreased.
- Chronic noise exposure at mild intensities will induce changes in hormonal regulation, if the individual threshold of allostasis is exceeded. A chronic allostatic load leads to subtle but significant changes in hormonal regulation, which are at present not fully understood.

EFFECTS OF PRENATAL NOISE EXPOSURE ON THE SENSITIVITY TO STRESS

Pregnant rats were subjected to noise and light stress, three times weekly on an unpredictable basis throughout gestation (Weinstock et al., 1998). Blood concentrations of adrenaline, noradrenaline and cortisol at rest and after footshock were assessed. At rest cortisol was significantly increased in offspring of stressed rats in comparison to controls while adrenaline and noradrenaline did not differ in either of the groups. After footshock, noradrenaline was significantly higher in offspring of stressed rats, showing that prenatal stress can induce long-term changes in the sensitivity of the sympathicoadrenal system to stress.

Pregnant monkeys were repeatedly exposed to unpredictable noise during days 90–145 after conception (Clarke et al., 1994). Blood concentration of ACTH and cortisol were measured in offspring of stressed and control monkeys at rest and under four progressively stressful conditions. Prenatally stressed offspring showed higher ACTH than controls in all four stressful conditions while cortisol did not change under stress. These results indicate that prenatal stress may have long-term effects on the HPA axis regulation.

EFFECTS OF NOISE EXPOSURE ON CORTISOL AND THE IMMUNE SYSTEM

The effect of acute noise stress on rats was studied by assessing blood concentrations of cortisol and total as well as differential leukocyte count (Archana and Namasivayam, 1999). A significant increase in cortisol and a significant decrease of total leukocyte counts were found.

Rats were exposed to “rock” music (80dB) for 24 hours (McCarthy, Quimet and Daun, 1992). In vitro stimulation of leukocyte subpopulations revealed several noise effects. Neutrophils and macrophages secreted significantly less superoxide anion and interleukin-1. Such effects may be detrimental to wound healing.

Pregnant rats were from gestation day 15 to day 21 daily exposed to the noise of a fire alarm bell ($L_{Amax} = 85-90$ dB) delivered randomly for 1 hour (Sobrian et al., 1997). In developing offspring mitogen-specific alterations in lymphoproliferatic activity and reduced immunoglobulin G levels were found at postnatal day 21.

Aguas et al. (1999) exposed a special breed of mice to low frequency noise – a model of noise – for three months as described below (Castelo Branco et al., 2003). These mice spontaneously developed an autoimmune disease at 6 months of age. Chronic low frequency noise exposure accelerated the expression of the autoimmune disease and affected the immune system, which was associated with kidney lesions and increased mortality.

Embryotoxic effects

Geber (1973) exposed pregnant rats day and night for three weeks to constantly changing sound mixtures between 76 and 94 dB for 6 minutes per hour, day and night, and demonstrated embryotoxic effects, notably calcification defects in the embryos.

Pregnant rats on a moderately magnesium deficient diet were exposed to noise during their active phase from 20.00 to 08.00 for three weeks (stochastically applied white noise impulses L_{Amax} : 87 dB, L_{eq} : 77 dB, t : 1 s duration) (Günther et al. 1981).

As compared to controls on the same diet, there was no difference in bone mineralization. The only significant effect was an increased fetal resorption rate.

The noise was changing in Geber's experiment but the noise level was comparable to the noise impulses stochastically applied by Günther et al. ($L_{Amax} = 87$ dB). Since these impulses were more frequent, their stress effect was at least as strong as the noise exposure employed by Geber. Therefore the major factor that differentiated the two exposure types in causing a reduced mineralization of the rat skeletons (Geber, 1973) must have been the additional noise exposure during sleep.

Castelo Branco et al. (2003) studied Wistar rats born under low frequency noise exposure. The third octave level of the applied broadband noise was > 90 dB for frequencies between 50 and 500 Hz. The broadband level was 109 dB(lin). The exposure schedule was chosen as a model for occupational noise: 8 hours per day, 5 days per week, and weekends in silence. Third generation rats born in low frequency noise environments were observed showing teratogenic malformations including loss of segments.

Morphological alterations in the myocardium caused by acute noise

Gesi et al. (2002a) reviewed the literature and stated that in experimental animals undergoing noise exposure, subcellular myocardial changes have been reported, especially at mitochondrial level; in particular, after 6 hours of exposure only the atrium exhibited significant mitochondrial alterations, whereas after 12 hours as well as subchronic exposure both atrium and ventricle were damaged.

Exposure of rats to 100 dB(A) noise for 12 hours caused a significant increase of DNA damage accompanied by ultrastructural alterations and increased noradrenaline concentrations in the myocardium (Lenzi et al., 2003). In another paper this group described an increase in mitochondrial calcium (Ca) influx caused by the same noise exposure. They described Ca accumulation at myocardial subcellular level. Summing up their results they wrote that: moreover, the present results joined with previous evi-

dence indicate that calcium accumulation is the final common pathway responsible for noise-induced myocardial morphological alterations (Gesi et al., 2000).

Connective tissue proliferation

Hauss, Schmitt and Müller (1971) described a proliferation of connective tissue in the myocardium of rats under acute exposure to noise.

On the basis of these results a noise exposure experiment was carried out of 5 weeks with day and night exposure to stochastically triggered bells (L_{Amax} : 108 dB, t (duration of one signal): 1 s, L_{eq} : 91 dB) (Ising, Noack and Lunkenheiner, 1974). We confirmed the results of Hauss, Schmitt and Müller (1971) using an electron microscope to demonstrate fibrosis in the interstitial tissue of the myocardium. Additionally electron dense areas (visible as black spots) located within bundles of collagen in the myocardium were observed. According to Selye (1962), these dark areas were most probably caused by high concentrations of calcium (Ca) carbonate or calcium phosphate deposits. This suggestion is consistent with the results of Gesi et al. (2000).

After publication of these findings, a reservation was correctly voiced that, as the noise exposure had not left intervals for sleep, it was not certain whether the myocardial damage was provoked by the noise stress as such or by a noise-induced lack of sleep. For this reason, all subsequent experiments provided for noise-free intervals of 8 to 12 hours during the rats' inactive phases to enable them to sleep.

Rats were exposed for 28 weeks to a random series of white noise impulses from 16.00 to 08.00 daily with an 8 hour rest in their inactive phase (Ising et al., 1979). The third octave spectrum of the noise was flat between 5 and 25 kHz and had a third octave level of 88 dB (lin) (broadband L_{Amax} = 97 dB(lin). L_{eq} = 87 dB(lin)). The duration of noise impulses was 4 seconds and the noise to pause ratio 1:10 on average. There was a small but significant increase in hydroxyproline as indicator of collagen in the rats' left myocardium. Electron micrographs showed, similar to the earlier experiment, collagen bundles in the otherwise empty interstitial space but no indication of calcium deposits.

Respiratory effects

Castelo Branco et al. (2003) studied respiratory epithelia in Wistar rats born under low frequency noise exposure and further exposed for up to 5403 hours during more than 2.5 years. The third octave level of the applied broadband noise was > 90 dB for frequencies between 50 and 500 Hz. The broadband level was 109 dB(lin). The exposure schedule was chosen as a model for occupational noise: 8 hours per day, 5 days per week and weekends in silence. Rats were gestated and born under the described noise exposure with additional exposures from 145 to 5304 hours. Transmission electron micrographs of the tracheal epithelium of rats exposed for 2438 hours revealed a subepithelial layer of hyperplastic collagen bundles, several of them exhibiting a degenerative pattern. The results indicate an increased proliferation as well as degenerative processes of collagen.

Castelo Branco et al. (2003) observed sheared cilia in the respiratory epithelia of Wistar rats born under and further chronically exposed to low frequency noise. As interpretation of their findings they stated that both mechanical and biochemical events may be responsible for this pattern of trauma.

Electrolytes: Ca/Mg shift

Acute exposure of rats to the fast rising overflight noise of low flying fighter planes

reaching levels of up to 125 dB(A)) (Ising et al., 1991; Ising, 1993) resulted not only in an increase of cortisol but also in a decrease of intracellular magnesium (Mg) and an increase of Mg excretion.

In guinea pigs, acute stress – due to 2 hours of noise exposure (95 dB white noise) or to overcrowding in the cage – caused significant increases of serum Mg and decreases of erythrocyte Mg (Ising et al., 1986).

For chronic noise experiments an additional stress factor had been sought which would act synergistically with unwanted noise, since in the above described noise experiment, half a year of exposure led to but relatively mild health effects (Ising et al., 1979). The justification for using two stressors derives from the fact that humans have to cope with a whole range of more or less synergistic stress factors and not with noise alone.

Organic damage as a result of chronic stress is likely to occur only under the condition that the overall exposure to stress exceeds a certain tolerance level during a relatively long period of time (Selye, 1974). For technical reasons, the two options available to supply a suitable additional stress factor were the cold or a magnesium (Mg) deficiency. Both factors, like habitual noise, cause an increased noradrenaline secretion. For practical reasons different degrees of a magnesium-deficient diet were selected as an additional stress factor. Noise exposure was provided by electro-acoustically reproduced traffic noise of L_{Amax} : 86 dB, L_{eq} : 69 dB over 12 hours during the rats' active phase. For one group the noise level was slightly increased (L_{eq} : 75 dB). The experiment lasted 16 weeks (Günther, Ising and Merker, 1978). Magnesium deficiency combined with noise exposure led to dose-dependent increases in adrenaline and noradrenaline, which can be used to quantify the overall stress of the dietary treatment. As stress grew, the hydroxyproline (as an indicator of collagen) and calcium (Ca) content of the myocardium increased while the magnesium content decreased. Long-term stress therefore resulted in an intracellular Ca/Mg shift.

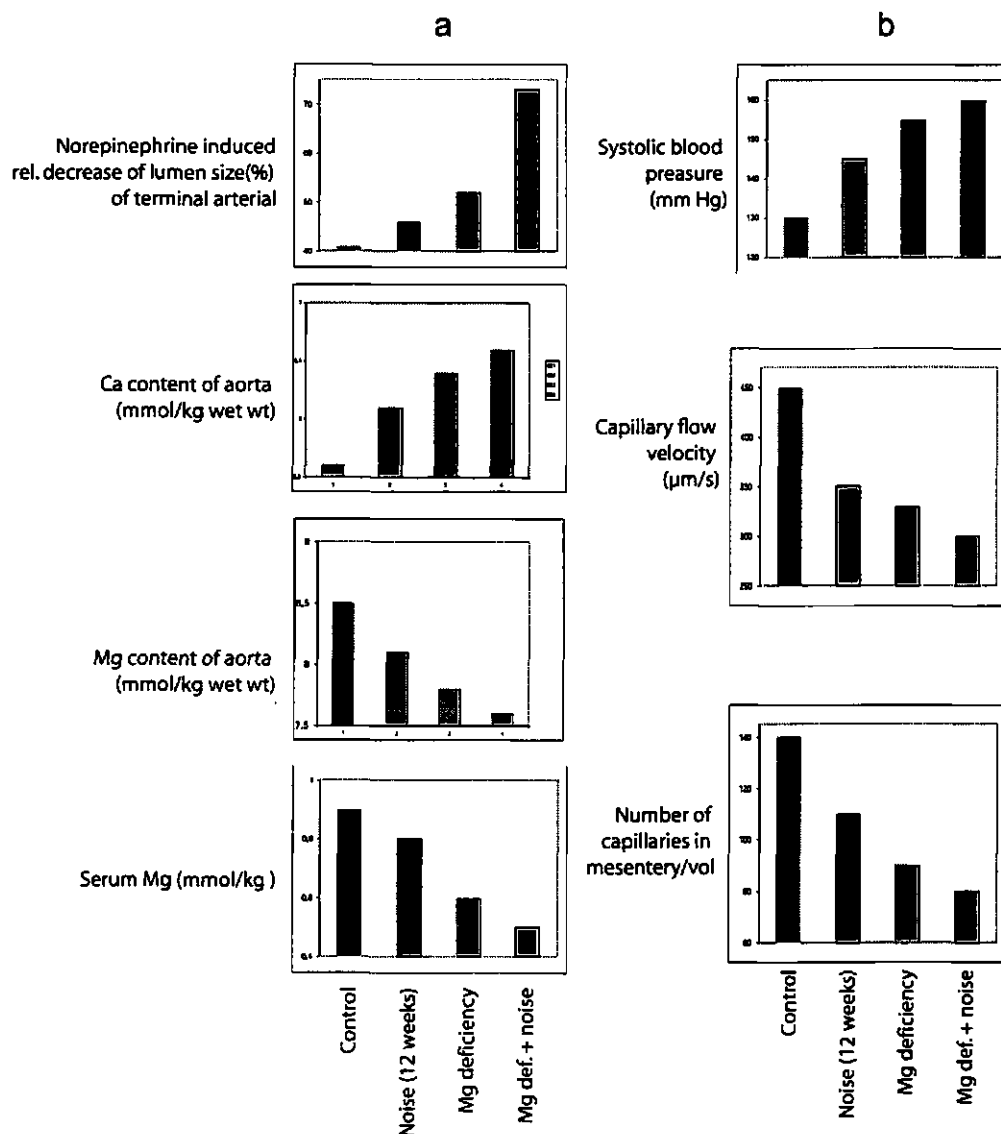
Altura et al. (1992) studied the relationship between microcirculation (measured several days after termination of noise exposure), hypertension and Ca/Mg shifts in vascular walls of noise-stressed rats on Mg deficient diets. Noise exposure during the first 8 weeks was set to an energy equivalent level of 85 dB(A) from 20.00 to 08.00. Noise impulses were randomly switched on at randomized peak levels of 80, 90 and 100 dB(A). During the final 4 weeks the equivalent noise level was elevated to 95 dB(A) and the daily exposure increased to 16 hours with an 8 hour rest during the animals' inactive phase. In aortic and port vein smooth muscle the Ca content increased with rising noise exposure, with decreasing Mg uptake, and with the combination of both together, while the Mg content decreased. Parallel to this the reactivity of terminal arterioles to noradrenaline was increased (Fig.1a).

Stress-induced Ca/Mg shifts in smooth muscle cells have the potential to increase the risk of hypertension and myocardial infarction (Ising, Havestadt and Neus, 1985). Stress increases the membrane permeability of catecholamine-sensitive cells, which in turn raises Ca influx into cells and liberates intracellular Mg. A depression of catecholamine-induced vasoconstriction by stress-dependent hypermagnesemia (excess serum Mg concentration) has been demonstrated experimentally. However, the benefit from this stress-depressing hypermagnesemia is obtained at the expense of increased renal Mg loss. In the long run, chronic stress combined with suboptimal Mg in diet will reduce the Mg release in acute stress situations, causing an increase of vasoconstriction and raising the risk of hypertension.

Fig.1

Effects of 12 weeks noise exposure, Mg deficient diet and the combination of both in Wistar rats. (a) Ca/Mg shifts in vascular smooth muscle, Mg concentration in blood and reactivity of arterioles to noradrenaline.

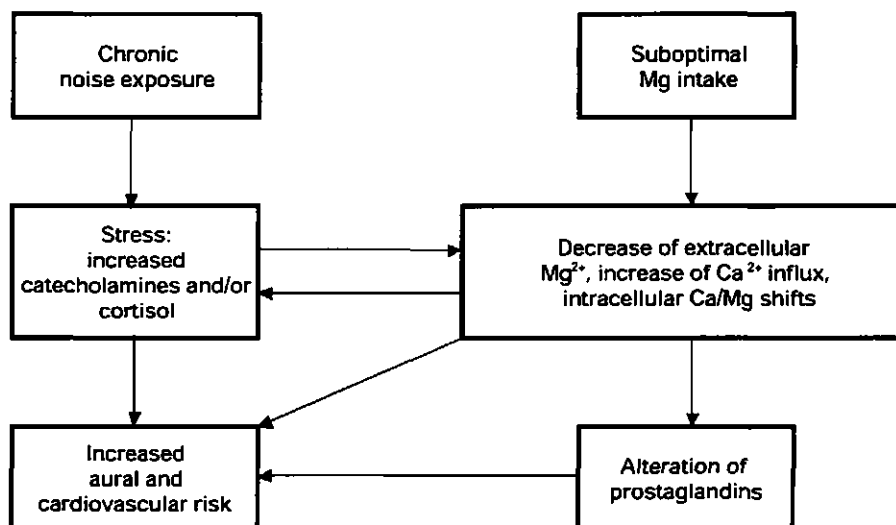
(b) Systolic BP, capillary blood flow velocity and numbers of capillaries/volume.



Source: Altura et al., 1992

Further analysis of the experimental results led to an interaction model between chronic stress and intracellular electrolyte shifts (Ising, 1981; Ising et al., 1986) (Fig.2). Chronic stress caused a loss of extracellular and intracellular Mg and an increase in intracellular Ca (Günther, Ising and Merker, 1978). A decrease of Mg was correlated with an increase in physiological noise sensitivity, that is, to more severe noradrenaline releases in animals and humans under noise exposure (Günther, Ising and Merker, 1978; Ising, Havestadt and Neus, 1985; Ising et al., 1986). There was a positive feedback mechanism between stress – caused by noise and other stressors – and intracellular Mg/Ca shifts, which may end in a circulus vitiosus and increase cardiovascular risks.

Fig. 2
Interaction between stress and
Ca/Mg shifts and its long term
consequences



Hypertension

Rothlin, Cerletti and Emmenegger (1956) exposed rats for 1.5 years, day and night, to 90 dB "audiogenic stress" and observed a raising of systolic BP values from 120 mm Hg to about 150 mm Hg. He used a cross-breed of Albino rats and wild Norwegian rats since Albino rats did not develop hypertension under noise exposure. After termination of exposure the BP returned to normal.

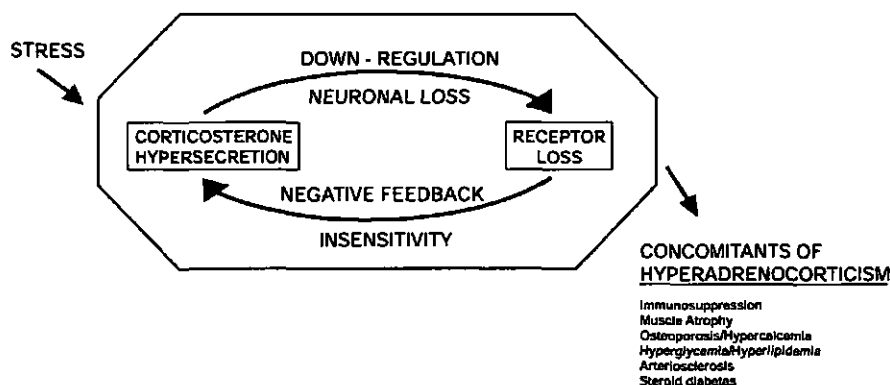
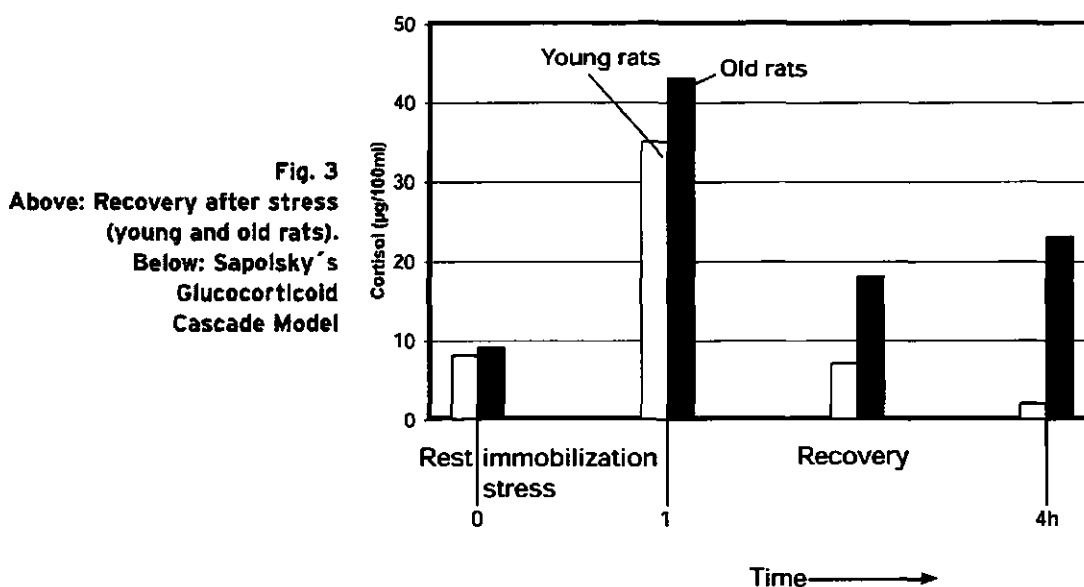
Albino rats were exposed to noise during their whole lifespan (for review see Borg, 1981) to periodic noise impulses of 80 and 100 dB. This periodic exposure had no detrimental health effects, which can be understood on the basis of the work of Glass, Singer and Friedmann (1969). Unpredictable noise presentation was shown to cause lasting cortisol increases in rats in contrast to periodic exposure to 100 dB, which led to adaptation (De Boer, van der Gugten and Slangen, 1989). The unpredictability of a noise is a decisive precondition of long-term stress effects.

Exposure of primates to traffic noise for 10 hours per day during 9 months led to a significant BP increase, which persisted during 3 weeks after termination of exposure (Peterson et al., 1981). A replication of this experiment with a different species of primates failed to show an increase of their BP (Turkkan, Hienz and Harris, 1983).

In the above-mentioned experiment of Altura et al. (1992), exposure to unpredictable noise impulses led within 12 weeks to irreversible changes of microcirculation and an increase of systolic BP (Fig. 1b). The observed rarefaction of capillaries in the mesentery can be interpreted as an indicator of accelerated ageing of the circulatory system.

Ageing and lifespan

The cortisol response and recovery after immobilization stress was compared in young and old rats. The results are demonstrated in Fig. 3 together with Sapolsky's Glucocorticoid Cascade Model (Sapolsky, Krey and McEwen, 1986). The stress response of young and old rats is more or less the same. However, while the young rats recover immediately after termination the old ones recover only in part.



Therefore, acute stress leads, in old animals, to considerably prolonged cortisol increases. On the other hand, chronically repeated stress activates the HPA axis and can cause cortisol receptor losses even in younger animals, a process generally developing only in old age. Finally, chronic cortisol hypersecretion may occur along with follow-up health defects.

Aguas et al. (1999) exposed a special breed of mice to the above described model of occupational low frequency noise for three months. Chronic low frequency noise exposure accelerated the expression of the autoimmune disease and was associated with kidney lesions and increased mortality.

Chronic noise exposure of animals on a suboptimal Mg diet led to increases of connective tissue and calcium and decreases of Mg in the myocardium (Günther, Ising and Merker, 1978). These changes were correlated with noradrenaline changes. Since they are also correlated with normal ageing, the noise stress induced changes may be interpreted as accelerated ageing (Ising, Nawroth and Günther, 1981). Even the lifespan was reduced in rats on an Mg deficient diet, and was further dose-dependently reduced in combination with noise exposure (see Table 1).

Table 1
Effects of noise exposure combined with
dietary Mg-deficiency in rats

Treatment		Effect				
4 months	3 months	Urine		Myocardium		Death rate
Mg in diet	Noise	Noradrenaline	Adrenaline	Hydroxyproline	Ca	Mg
	L_{eq}/L_{Amax}	($\mu\text{g/g Cre}$)		(mg/g dry wt.)	(mg/g d.w.)	(mg/g d.w.)
control	ambient	18 \pm 4	12 \pm 2	3.0 \pm 0.1	3.0 \pm 0.2	37.5 \pm 0.8 0
suboptimal	ambient	23 \pm 4	18 \pm 2	3.0 \pm 0.1	3.5 \pm 0.5	38.0 \pm 1.7 0
suboptimal	69/86 dB	37 \pm 11	16 \pm 2	3.0 \pm 0.1	4.3 \pm 0.2	37.9 \pm 1.3 0
deficient	ambient	98 \pm 17	20 \pm 5	3.9 \pm 0.1	6.2 \pm 0.7	31.2 \pm 1.4 38%
deficient	69/86 dB	129 \pm 19	41 \pm 10	4.6 \pm 0.1	6.7 \pm 0.6	29.8 \pm 1.8 62%
deficient	75/86 dB	172 \pm 26	60 \pm 15	5.6 \pm 0.9	8.0 \pm 0.9	26.8 \pm 0.8 75%

Adrenaline and noradrenaline excretion was measured during the fourth week of noise exposure; death rate is related to the 4-month period of Mg treatment; all other parameters were determined at the end of the experiment (mean values \pm S.E.). Noise has the potential to cause stress reactions which are enhanced by suboptimal magnesium intake. Chronic noise-induced stress accelerates the ageing of the myocardium and thus increases the risk of myocardial infarction. The involved pathomechanisms include increases of catecholamines and/or cortisol under acute noise exposure and an interaction between endocrine reactions and intracellular Ca/Mg shifts.

WHAT CAN BE LEARNED FROM ANIMAL STUDIES ABOUT NOISE EFFECTS IN HUMANS?

The effects of low frequency noise – the “vibroacoustic disease” – were studied primarily in humans (for review see Castello Branco and Alves-Pereira, 2004).

In this context, the amygdalar contribution to conditioned fear learning, revealed for normal human subjects, has to be mentioned. Longer lasting activation of the HPA axis, especially abnormally increased or repeatedly elevated cortisol levels may lead to disturbances of the hormonal balance and even severe diseases in man (Spreng, 2000).

Catecholamines induce various detrimental effects on the heart (Ceremuzynski, 1981). Additionally, magnesium deficiency causes alterations of serum lipids (Weglicki et al., 1993), cytokines (Rayssiguier, 1990) and prostaglandines (Nigam, Averdunk and Günther, 1986), in particular an increase of thromboxan, which is released from thrombocytes (Neumann and Lang, 1995) and several other cell types and – in turn – thromboxan A₂ can aggregate thrombocytes. All these alterations may increase the risk of myocardial infarction.

Beside these cardiovascular stress effects, chronically increased cortisol may induce

neuronal degeneration and thus accelerate the ageing also of the brain (Sapolsky, Krey and McEwen, 1986), not only in rats but in humans as well (Sapolsky, 1994).

The importance of Ca/Mg shifts was confirmed by post mortem studies of hearts from victims of IHD (Elwood et al. 1980). The tissue samples were taken from areas of the myocardium not affected by the infarction and the results were stable after controlling for several confounders. The results are shown in Table 2. With normal ageing Ca increases and Mg decreases in the myocardium. This process is accelerated in myocardial infarction patients, which indicates an accelerated ageing of these peoples' heart muscle under the pathogenic influences that lead to myocardial infarction.

Table 2
Age dependency of myocardial Ca and Mg
contents in Ischaemic heart disease (IHD)

IHD deaths and non IHD deaths. (Mean Value \pm SD, numbers in brackets)

	Group	Age < 45years	45-64 years	≥ 65 years
Ca [$\mu\text{g/g}$]	Non IHD	43 \pm 15 (175)	50 \pm 14 (281)	57 \pm 22 (155)
	IHD	48 \pm 10 (48)	53 \pm 17 (389)	58 \pm 21 (188)
Mg [$\mu\text{g/g}$]	Non IHD	183 \pm 28	173 \pm 34	178 \pm 30
	IHD	170 \pm 29	157 \pm 30	156 \pm 27
Ca/Mg	Non IHD	0.24	0.29	0.32
	IHD	0.28	0.34	0.37

Another factor which decreases Mg and increases Ca (Hofecker, Niedermüller and Skalicky, 1991) and collagen (Caspari, Gibson and Harris; 1976, Anversa et al., 1990; Gibbons, Beverly and Snyder, 1991) in the myocard is normal ageing (Ising, Nawroth and Günther, 1981). Therefore, it is plausible that the age-dependent decrease of Mg in hearts of IHD victims was about double of that in age-matched non-IHD deaths. This is therefore an indication that age- and stress-dependent electrolyte changes exist in humans and may be correlated with an increased risk of IHD.

Long-term experiments with Mg-deficient and noise-stressed rats showed that connective tissue and Ca in the myocardium increased with age while Mg decreased. Hence, stress caused by noise or cold is enhanced by suboptimal Mg intake and accelerates the ageing of the heart and decreases the lifespan (Heroux, Peter and Heggteit, 1977; Ising, Nawroth and Günther, 1981; Günther, 1991).

Since coronary arteriosclerosis increases strongly with age (Lakatta, 1990) a biologically older heart is at a higher risk of IHD and of myocardial infarction. The interaction process described seems to be one of the pathomechanisms by which chronic noise stress increases the risk of myocardial infarction.

Several of the risk factors described in the literature to explain the correlation of work stress with myocardial infarction have been found to be increased under noise-induced stress as well, that is, increases of BP and total cholesterol.

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APPENDIX 4. NOISE AND SLEEP IN CHILDREN

FACTORS THAT MODIFY AUDITORY AROUSAL THRESHOLDS IN CHILDREN

By the time that most studies were conducted in infants, it had become progressively evident that arousal and awakening thresholds are influenced by a variety of factors. These significantly modify the response to ambient noise of sleeping infants. Some factors inhibit the arousal response, while others enhance the response.

PRENATAL AND PERINATAL FACTORS

Age of gestation

In 97 healthy infants, auditory awakening thresholds decreased significantly from the 44th to the 60th week after conception (Kahn, Picard and Blum, 1986). Awakening thresholds were defined as the infant opening their eyes and/or crying. Mean awakening thresholds dropped from 98.5 ± 11 at the 44th week after conception to 83 dB(A) by the 60th week after conception.

Cigarette smoke

To evaluate the effects of cigarette smoke on polygraphic arousal thresholds, 26 newborns were studied with polygraphic recordings for one night: 13 were born to mothers who did not smoke, and 13 were born to mothers who smoked (over 9 cigarettes per day) (Franco et al., 1999). Another group of infants with a median post-natal age of 12 weeks were also studied: 21 born to non-smoking mothers and 21 born to smoking mothers. The auditory arousal thresholds of the infants of both age groups were measured with the use of auditory challenges of increasing intensity, administered during REM sleep. More intense auditory stimuli were needed to induce arousals in newborns ($p=.002$) and infants ($p=.044$) of smokers than in infants of non-smokers (mean value of 84 ± 11 dB(A) for smokers and 81.6 ± 20 for non-smokers). Behavioural awakening (infants opening their eyes and/or crying) occurred significantly less frequently in the newborns of smokers ($p=.002$) than of non-smokers.

It was concluded that newborn and infants born to smoking mothers had higher arousal thresholds to auditory challenges than those born to non-smoking mothers. From the present findings, it appeared that the impact of exposure to cigarette smoke occurred mainly before birth.

POSTNATAL FACTORS

The following postnatal factors modify arousal from sleep.

Sleep stage

In infants, auditory stimuli have generally indicated increased responses during active as compared with quiet sleep (Busby, Mercier and Pivik, 1994).

Time of the night

In 31 infants, the arousal thresholds decreased across the night (mean value of 67 ± 12.5 dB(A) in the first part of the night, for 51 ± 3.5 in the third part of the night; $p=.017$) (Franco et al., 2001). Similar findings had been reported in adult subjects (Rechtschaffen, Hauri and Zeitlin, 1966).

Body position during sleep

To investigate whether prone or supine sleeping was associated with a different response threshold to environmental stimuli, 25 3-month-old healthy infants with a median age of 9 months were exposed to an auditory challenge while sleeping successively prone or supine (Franco et al., 1998). Three infants were excluded from the study because they awoke while their position was being changed. For the 22 infants included in the analysis, more intense auditory stimuli were needed to arouse the infants in the prone position (median of 70 dB(A), range values 50 to more than 100 dB(A)) than in the supine position (median of 60 dB(A), range values 50–90 dB(A)) ($p=.011$). Arousal thresholds were higher in the prone than in the supine position in 15 infants, unchanged in 4 infants and lower in the prone position in 3 infants ($p=.007$). It was concluded that infants show higher arousal thresholds to auditory challenges when sleeping in the prone position than when sleeping in the supine position. The findings could not readily be explained. The difference in arousal thresholds could be related to difference in chest wall mechanoreceptor responses, or differences in BP and/or central baroreceptors responses.

Ambient room temperature

Two groups of healthy infants with a median age of 11 weeks were recorded polygraphically during one night: 31 infants were studied at 24°C and 31 infants at 28°C . To determine their arousal thresholds, the infants were exposed to white noises of increasing intensities during REM and non-REM sleep (Franco et al., 2001). The arousal thresholds decreased across the night in the infants sleeping at 24°C ($p=.017$). The finding was not found for the infants sleeping at 28°C . When analysing the arousal responses according to time of the night, it was found that the auditory thresholds were significantly higher at 28°C (75 ± 19 dB(A)) than at 24°C (51 ± 3.5 dB(A)) between 03.00 and 06.00 ($p=.003$). These findings were only seen in REM sleep.

Sleeping with the head covered by bedclothes

To evaluate the influence of covering the face of sleeping infants with a bed sheet, 18 healthy infants with a median of 10.5 weeks (range 8–15 weeks) were recorded polygraphically for one night (Franco et al., 2002). They slept in their usual supine position. During sleep, a bed sheet was gently placed on their face for 60 minutes. With the face free or covered by the sheet, the infants were exposed to white noises of increasing intensities during REM and non-REM sleep. Compared to with their face free, during the periods when their faces were covered, the infants had increases in pericephalic ambient temperature ($p<.001$), increases in REM sleep ($p=.035$) and body movements ($p=.011$) and a decrease in non-REM sleep ($p<.001$). Respiratory frequency was increased in both REM ($p=.001$) and non-REM ($p<.001$) sleep. With their face covered, the infants had higher auditory arousal thresholds (mean of 76 ± 23 dB(A)) than with their face free (mean of 58 ± 14 dB(A)) ($p=.006$). The difference was seen in REM sleep only. A positive correlation was found between pericephalic temperature and arousal thresholds in REM sleep ($r=.487$; $p=.003$).

Short sleep deprivation

Following short sleep deprivation, a study reported that in infants there was no measurable change in arousal propensity by auditory stimuli (1 kHz pure tone, delivered in the midline of the cot, from 73 dB and increased in 3 dB steps to 100 dB)

during quiet sleep (Thomas et al., 1996). Another study was undertaken to evaluate the influence of a brief period of sleep deprivation on sleep and arousal characteristics of healthy infants (Franco et al., submitted). Thirteen healthy infants with a median age of 8 weeks (range 7–18 weeks) were recorded polygraphically during a morning nap and an afternoon nap in a sleep laboratory. They were two hours sleep-deprived, either in the morning or in the afternoon before being allowed to fall asleep. Six infants were sleep-deprived before the morning nap and seven before the afternoon nap. During each nap, the infants were exposed to white noises of increasing intensities in REM sleep to determine their arousal thresholds. Following sleep deprivation, the infants tended to have less gross body movements during sleep ($p = .054$). They had a significant increase in obstructive sleep apnoeas ($p = .012$). The infants' auditory arousal thresholds were significantly higher following sleep-deprivation (mean of 76 ± 13.5 dB(A)) than during normal sleep (mean of 56 ± 8.4 dB(A)) ($p = .003$) and during REM sleep. It was concluded that short-term sleep deprivation in infants is associated with the development of obstructive sleep apnoeas and a significant increase in arousal thresholds.

Pacifiers and breastfeeding

Fifty-six healthy infants were studied polygraphically during one night: 36 infants used a pacifier regularly during sleep; 20 never used a pacifier (Franco et al., 2000). Thumb users or occasional pacifier users were not included in the study. The infants were recorded at a median age of 10 weeks (range 6–19 weeks). To evaluate their auditory arousal thresholds, the infants were exposed to white noise of increasing intensity during REM sleep. Polygraphic arousals occurred at significantly lower auditory stimuli in pacifier-users than in nonusers (mean of 60 ± 11.6 with pacifiers, for 71 ± 15.3 without pacifier; $p = .010$). Compared to non-users, pacifier-users were more frequently bottle-fed than breastfed ($p = .036$).

Among infants sleeping without a pacifier, breastfed infants had lower auditory thresholds than bottle-fed infants (mean of 67.7 ± 13.0 breastfed, for 77.7 ± 17.5 bottle-fed; $p = .049$). The question of how a pacifier contributes to protect the sleeping infant might be best explained by the observed loss of the pacifier early after sleep onset. This could contribute to disruption of the infant's sleep and favour arousals.

CONCLUSIONS

Various factors modify auditory arousal responses from sleep in healthy infants. Some inhibit arousals while others enhance the response. To evaluate the effect and dose-effect relationship on children therefore requires the careful determination of confounders that may bias studies and lead to conflicting results.

Additional confounders should be added to the list of factors that modify arousal thresholds. These include past experience with the stimulus (Rechtschaffen, Hauri and Zeitlin, 1966), or the presence of meaning in the noise as both of them are of critical importance in determining the persistence of physical reactions to the noise (McLean and Tarnopolsky, 1977). These are the reasons which lead most sleep/wake researchers to use white noises to stimulate the sleeping child.

Knowledge of these variables does little to clarify the physiological determinants of the awakening response, because knowledge of how such variables are related to possible physiological determinants is little better than that of the awakening response itself (Rechtschaffen, Hauri and Zeitlin, 1966).

These findings however, underline the significant dose-response relationship between ambient noise and arousal or awakening from sleep in infants.

NOISE AND SLEEP FOR DIFFERENT STAGES OF DEVELOPMENT

THE FETUS

The human fetus spends most of its time in a state equivalent to sleep, similar to that recorded in newborn infants. The healthy fetus in utero was shown to react to external noises. This is the result of the development of the human cochlea and peripheral sensory end organs. These complete their normal development by 24 weeks of gestation. Sound is well transmitted into the uterine environment. Ultrasonographic observations of blink/startle responses to vibroacoustic stimulation are first elicited at 24–25 weeks of gestation, and are consistently present after 28 weeks, indicating maturation of the auditory pathways of the central nervous system (Committee on Environment Health of the American Academy of Pediatrics, 1997). The fetus reacts to 1–4 seconds of 100–130 dB of 1220–15000 Hz sound. The hearing threshold (the intensity at which one perceives sound) at 27–29 weeks of gestation is approximately 40 dB and decreases to a nearly adult level of 13.5 dB by 42 weeks of gestation, indicating continuing postnatal maturation of these pathways.

Teratogenic effects have been described in animals prenatally exposed to noise (Committee on Environment Health of the American Academy of Pediatrics, 1997). These were associated with higher levels of cortisol and corticotropin hormones in the exposed animals. No such effects could be demonstrated in humans, in whom studies on the relation between exposure to noises during gestation and shortened gestation or lower birth weights were inconclusive or conflicting. It is possible that in these studies, noise could be a marker of other risk factors (Committee on Environment Health of the American Academy of Pediatrics, 1997). In conclusion, most studies on the effects of noise on perinatal health have been criticized as being hampered by serious methodological limitations, both in terms of the measurement of exposure and outcome, and failure to control for other known determinants of the outcomes under investigation. The lack of properly controlled studies makes it difficult to draw conclusions about what effects ambient noise has on perinatal outcomes (Morrell, Taylor and Lyle, 1997).

NEWBORN INFANTS

A large number of investigations have been concerned with the responses of sleeping newborn infants to acoustic signals. Many of the studies arise from a large and general interest in child development as well as from a need for hearing tests for infants (Mills, 1975).

Infant incubators produce continuous noise levels of between 50 and 86 dB(lin) (American Academy of Pediatrics, 1974). Oxygen inlets produced an additional 2 dB (lin). Slamming of incubator doors and infant crying produced 90 to 100 dB(A).

(American Academy of Pediatrics, 1974). It was shown that inside incubators, background noise level is about 50 dBA and can reach 120 dBA (Committee on Environment Health of the American Academy of Pediatrics, 1997). Much of the energy is located below 500 Hz, between 31 and 250 Hz (Mills, 1975).

Ambient noise appears to influence the quantity and quality of the sleep of newborns. Some newborns appear to be particularly responsive to ambient noises. Sleeping premature, anoxic, or brain-damaged infants detect intruding sounds better than sleeping healthy or term babies (Mills, 1975).

Newborn infants spend most of their time sleeping. Some studies have documented hearing loss in children cared for in intensive care units (Committee on Environment Health of the American Academy of Pediatrics, 1997). Noise and some ototoxic drugs act synergistically to produce pathological changes of the inner ears of experimental animals (neomycin, kanamycin, sodium salicylate). The relationship with the infant's clinical condition and associated treatments has, however, not yet been clearly defined. Infants exposed to sound levels of incubators are usually premature, on drugs and in very poor health. Moreover, the exposures are continuous. A weak infant could spend weeks sleeping in such a noise level without rest periods away from noise (Mills, 1975).

High noise levels may be associated with other types of responses. In young infants, sudden loud (of approximately 80 dB) environmental noise induced hypoxaemia.

Noise reduction was associated in neonates with increases in sleep time, in particular in quiet sleep (Committee on Environment Health of the American Academy of Pediatrics, 1997). It also resulted in fewer days of respiratory support and oxygen administration. Premature infants cared for with noise reduction had a better maturation of electroencephalograms.

A Committee on Environmental Health of the American Academy of Pediatrics (1997) concluded that high ambient noise in the neonatal intensive care unit (NICU) changed the behavioural and physiological responses of infants. For all the above observations and considerations, sound in infant intensive care units should be maintained at under 80 dB(A) (Graven, 2000). Among other recommendations, paediatricians were encouraged to monitor sound in the NICU, and within incubators, where a noise level greater than 45 dB is of concern.

INFANTS (1 MONTH TO 1 YEAR OLD)

Some studies of the effect of external noises on the sleep/wake reactions of infants were conducted in their natural home environment. The reactions of babies to aircraft noise were studied by means of electroplethysmography (PLG) and EEG (Ando and Hattori, 1977). The recordings were done in the morning, in the infants' sleeping rooms. The infants were exposed to recorded noise of a Boeing 727 at take-off. The noise was presented at 70, 80 and 90 dB(A) at peak level at the position of the babies' heads. The subjects who had not been awakened by exposure to aircraft noise were exposed to music (Beethoven's Ninth Symphony) at levels of 70, 80 and 90 dB(A). The frequency ranged between 100 Hz and 10 kHz. It was found that the babies whose mothers had moved to the area around the Osaka International Airport before conception (Group I; n=33) or during the first five months of pregnancy (Group II; n=17) showed little or no reaction to aircraft noise. In contrast,

babies whose mothers had moved closer to the airport during the second half of the pregnancy or after birth (Group III; $n=10$ or IV; $n=3$) and the babies whose mothers lived in a quiet living area (Group V; $n=8$) reacted to the same auditory stimuli. The babies in groups I and II showed differential responses depending on whether the auditory stimuli were aircraft noise or music. Abnormal PLG and EEG were observed in the majority of babies living in an area where noise levels were over 95 dB(A). It was concluded that the difference in reactivity to aircraft noise may be ascribed to a prenatal difference in time of exposure to aircraft noise. The reactions diminished after the sixth month of life in groups I and II, and the ninth month in groups III to V. This phenomenon may be explained as habituation to aircraft noise after birth. However, in all groups, no habituation occurred for a noise level over 95 dB(A) (Ando and Hattori, 1977). This study was criticized, as the authors did not adjust for several important determinants of birth weight, such as prematurity and the mother's age, weight, smoking status or socioeconomic status (Morrell et al., 1997).

Noise levels may be constantly high in paediatric units. The mean noise levels measured in a centre of a surgical recovery room were 57.2 dB(A), while those measured at the patients' heads were 65.6 dB(A) (American Academy of Pediatrics, 1974). In a medical unit (6-bed wards containing 5 infants between 3 and 17 months) peak sound levels were recorded on the pillow of the cot for 12 min (Keipert, 1985). Infant crying produced 75–90 dB(A) and a beeper around 76–78 dB(A). Peak noise levels recorded at the nurses' station were about 78 dB(A) for telephone, 80 for infant crying, public address system, adult talking, and up to 90 dB(A) for child talking (Keipert, 1985).

In a study conducted on infants exposed to 50–80 dB(lin) in the range of 100–7000 Hz (American Academy of Pediatrics, 1974), a level of 70–75 dB(lin) for 3 minutes led to obvious disturbance or awakening in two thirds of the children. All infants awakened after 75 dB(lin) for 12 minutes.

In other studies conducted on the effects of awakening and arousal, it was shown that white noise intensity was significantly lower when it elicited polygraphically scored arousals than when it induced awakenings (Franco et al., 1998).

TODDLERS PREADOLESCENTS (8–12 YEARS OLD) ADOLESCENTS (13–18 YEARS OLD)

Developmental variations in auditory arousal thresholds during sleep were investigated in four groups of normal male subjects: children ($n=6$; 5–7 years old), preadolescents ($n=10$; 8–12 years old), adolescents ($n=10$; 13–16 years old), and young adults ($n=10$; 20–24 years old) (Busby, Mercier and Pivik, 1994). Arousal thresholds were determined during non-REM and REM sleep for tones (3-s, 1500 Hz pure tones delivered in an ascending series of increasing intensity, 5 dB increments beginning at 30 dB SPL (sound pressure level) re 0.0002 dynes/cm² until awakening or maximum intensity of 120 dB) presented via earphone insert on a single night following two adaptation nights of undisturbed sleep. Age-related relationships were observed for both awakening frequency and stimulus intensity required to effect awakening, with awakenings occurring more frequently in response to lower stimulus intensities with increasing age. In children, 43.1% of stimuli induced awakenings, in preadolescents 54.8%, adolescents 72% and adults 100% ($X^2=60.37$; $p<.001$). Partial arousals (brief EEG desynchronization and/or EMG activity with the subjects returning to sleep) occurred in 9.8% of children, 4.8% of preadoles-

cents, 12.2% of adolescents, 0% of adults. Although stimulus intensities required for awakening were high and statistically equivalent across sleep stages in non-adults, higher intensity stimulus was required in stage 4 relative to stage 2 and REM sleep. Frequency of awakening increased with age, whereas stimulus intensities required to effect these awakenings decreased with age. These relationships were maintained for individual sleep stages. These results confirm previous observations of marked resistance to awakening during sleep in preadolescent children and suggest that processes underlying awakening from sleep undergo systematic modification during ontogenic development. The observed resistance to elicited awakening from sleep extending up to young adulthood implies the presence of an active, developmentally related process that maintains sleep (Busby, Mercier and Pivik, 1994).

In another study, children aged 5–7 years were shown to be 10–15 dB less sensitive to pure tones than adults aged 22–30 (Mills, 1975). Another report on male hyperactive and normal children aged 8–12 showed that these children were awakened with auditory stimulus intensity levels of up to 123 dB SPL, much higher than values reported for adults (range of 50–85 dB) (Busby, Mercier and Pivik, 1994).

In a study on four children (two males), aged 5–8 years old on the effects of simulated sonic booms (68 dB(A) near the subjects' ears), 94.1% of the subjects showed no change, 5.9% had shallower sleep, but none aroused or had behavioural awakening. In general, the frequency of arousal or behavioural awakenings and of sleep stage changes increased with age (up to 75 years) (Lukas, 1975).

In a prospective longitudinal investigation, which employed non-exposed control groups, effects of aircraft noise prior to and subsequent to inauguration of a new airport as well as effects of chronic noise and its reduction at an old airport (6–18 months after relocation), were studied in 326 children aged 9–13 years (Bullinger et al., 1999). The psychological health of children was investigated with a standardized quality of life scale as well as with a motivational measure. In addition, a self-report noise annoyance scale was used. In the children studied at the two airports over three time points, results showed a significant decrease of total quality of life 18 months after aircraft noise exposure as well as motivational deficits demonstrated by fewer attempts to solve insoluble puzzles in the new airport area. Parallel shifts in children's attributions for failure were also noted. At the old airport parallel impairments were present before the airport relocation but subsided thereafter (Bullinger et al., 1999).

In some studies, the effects of ambient noise on autonomic responses could be demonstrated in children. In children aged 6–12 years exposed to intermittent traffic noise during 4 nights (at a rate of 90 noises per hour; peak intensity of the noise, 45, 55 and 65 dB(A) varied semi-randomly) and 2 quiet nights. Heart rate was affected and relatively higher in noise during REM and stage 2 than during delta sleep (Muzet et al., 1980, in Abel, 1990).

CONCLUSIONS

Several studies on the extra-auditory effects of ambient noise on sleeping children were summarized in Table 1. In relation to ambient noise, specific changes were reported in both sleep quality and quantity. Some of the effects were shown to have a dose-response relationship. Several limitations to the present report should be discussed. Firstly, no one knows

whether the inference that is often made that the effects of noise might develop with a longer exposure time (Abel, 1990) is correct. Serious cardiorespiratory or autonomic changes, such as increases in BP could only develop following a long time exposure starting from childhood. This, in fact, has never been documented, nor has the extent of variability between subjects due to difference in susceptibility. Secondly, there is no information to evaluate whether adaptation to ambient noise could limit the effects observed during short-term experiments. Thirdly, as the existing research data are applicable to generally healthy children, no one knows how the reported findings could be applied to ill children, children receiving medical treatment or very young premature infants. Finally, as most studies were conducted in laboratory controlled environments, no one knows the correlation between these studies and the effects of noise in the home. The multifactorial effects of the environment on sleep and arousal controls could be much more complex than expected. One might predict that, similarly as for adults, the effects of noise on the child's sleep and health are very complicated and depend upon the spectrum and level of the noise, temporal aspects of the noise, psychological responses to the noise and the nature of the evaluation technique. The complexity of the conditions related to sleep/wake controls was illustrated by the review of confounding factors affecting auditory arousal thresholds.

Despite these limitations, it can be concluded that, based on the evidence available, the extra-auditory effects of noise could be pervasive, affecting the children's physical and psychological well-being. Changes in sleep quantity and quality together with autonomic reactions are seen when a child is exposed to ambient noise during sleep. Ambient noise exerts a dose-effect relationship on changes in sleep/wake behaviours. These reflect modifications induced within the brain of the sleeping child. It remains, however, to be determined what pervasive effects long-term exposure to ambient noise has on the child's development, health and well-being. Evidence should also be defined to support an enforcement of strategies for noise reduction at the source as suggested by some studies. Noise-induced health effects on children, a clinical and public health concern, should be evaluated by further studies.

No.	dB(A)	% responses	Type of responses	Reference	Table 1 Arousal and awakening in children a review of the literature
1	80	70	Neonates motor response	Steinschneider 1967	
2	60	5	Neonates startle response	Gädeke et al., 1969	
70	10				
80	20				
100	60				
3	60	7	Neonates startle response	Ashton 1967	
65	10				
70	40				
4	80	70	Child awake	Semczuk 1967	
5	100	70	Child awake	Busby, Mercier and Pivik 1994	
6	100	76	Preadolescent awake		
7	100	86	Adolescent awake		
8	60	100	Adult		
9	120	72	Infant awake	Kahn, Picard and Blum, 1986	
10	75	75	Infant awake	Gädeke et al., 1969	

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Environmental noise is a threat to public health, having negative impacts on human health and wellbeing. This book reviews the health effects of night time noise exposure, examines dose effects relations, and presents interim and ultimate guideline values of night noise exposure. It offers guidance to policy-makers in reducing the health impacts of night noise, based on expert evaluation of scientific evidence in Europe.



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**World Health Organization
Regional Office for Europe**

Scherfigsvej 8, DK-2100 Copenhagen Ø, Denmark
Tel.: +45 39 17 17 17. Fax: +45 39 17 18 18. E-mail: postmaster@euro.who.int
Web site: www.euro.who.int